



Essential Oils: A “Potential Green” Alternative in Pharmaceutical, Nutritional and Agricultural Sectors

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Abstract

In the era of modern medicine, the therapeutic use of plant-derived essential oils has been one of the fascinating fields of study for researchers around the globe. The plant-derived essential oils, which are a combination of volatile organic compounds may be used as a substitute for the treatment of pathogenic microbes. The antimicrobial properties of essential oils are extremely diverse. In microbial infections, essential oils create an electrochemical gradient across the cell wall which intervenes with ATP synthesis and can also disrupt the electron transport system (ETS) by rupturing the mitochondrial membrane. Many essential oils have antiviral properties that can effectively treat COVID-19. The purpose of the current review is to shed light on the antimicrobial efficacy of essential oils. A survey of the methods used for the determination of the interaction and mechanisms involved in the antimicrobial activities of essential oils are also reported as well and the applications of essential oils could be interesting COVID-19 therapeutic options because of their pharmacological actions. This review will attract the attention of researchers to optimize and elucidate the use of essential oils as green alternatives to treat the deadliest infectious diseases in living organisms.

Keywords: antimicrobial, aromatherapy, antioxidant, COVID-19, essential oil, food preservative

1. INTRODUCTION

During the co-evolution of plant-animals, plants provided a limitless source of food, fibers and drugs. Nowadays, natural products play an important role in eco-friendly management. Naturally, plants can produce a broad range of molecules, especially secondary metabolites. In secretory cells, epidermal cells, cavities, canals, or glandular hair, these metabolites are located and stored, which are known to have a role in safeguarding plants against diseases that are naturally produced by plants [1][2]. Essential oils are complex mixtures of volatile hydrocarbons and oxygenated hydrocarbons that make them an important source of biologically active compounds that can be utilized as a beneficial substitute and ecological alternatives in place of synthetic and chemical items, which pose greater threats to the environment and human health. The market for

essential oils is anticipated to increase from 2021 to 2028 at a compound yearly growth rate of 7.4%, reaching USD 35.5 billion (according to the report of U.S. market CAGR) [3].

The search for new therapeutic alternatives has revealed that herbal extracts have potential antimicrobial actions. Essential oils or their main active compounds have been reported to possess a wide spectrum of antibacterial, antiviral, antifungal, antioxidant, antiparasitic, insecticidal, and cytotoxic properties [4]. The main components of essential oil can be differentiated into oxygenated compounds (alcohols, phenols, esters, aldehydes) and terpene hydrocarbons (monoterpenes, sesquiterpenes) that obstruct the physiological and biochemical processes involved in the development and multiplication of microorganisms [5]. The usage of organically produced antimicrobials has significantly expanded over the past ten years due to the trend of "green consumerism" that is currently sweeping society. This movement emphasizes the desire for products with less of an environmental impact and fewer synthetic food additives. On account of distinct physiochemical characteristics such as odors, color, solubility, refractive index, and specific gravity, with a wide range of biological activities, essential oils have acquired interest from the scientific community.

Bio-preservatives are a diverse group of organic substances that can be used to lower or completely eradicate disease populations while improving the

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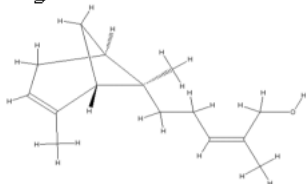
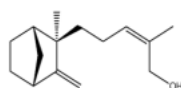
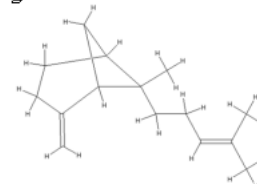
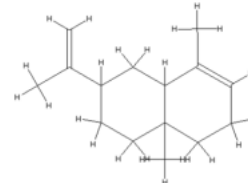
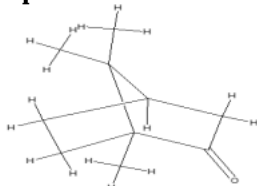
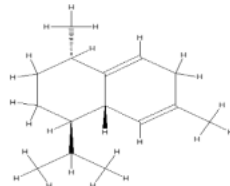
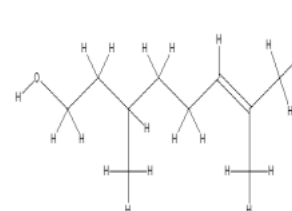
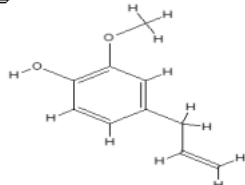
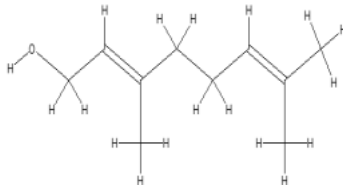
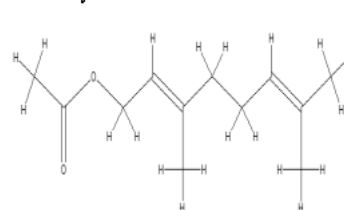
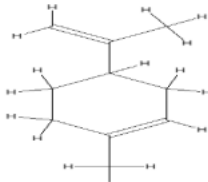
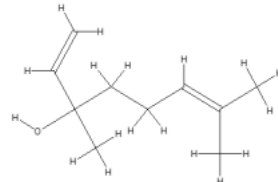
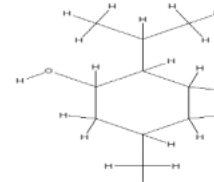
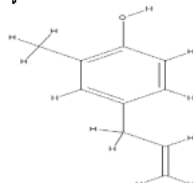
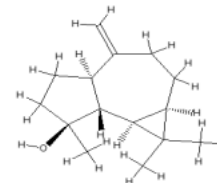
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Bergamotol**Beta-Santalol****Bergamotene****1,8-cineole****Borneol****Alpha-Selinene****Camphor****Cubenene****Citronellol****Eugenol****Geraniol****Geranyl acetate****Limonene****Linalool****Menthol****Methyl chavicol****Seychellene****Spathulenol****Figure 1.** Chemical composition and structure of essential oils [5].

quality of food. The use of essential oils as new alternative methods with high efficiency, economy and safety for controlling harmful cyanobacterial growth has received much more attention than to chemical agents. Furthermore, few researches on naturally available bioactive compounds with high capabilities for controlling dangerous cyanobacterial blooms are available and critically

analyzed. The primary mechanisms by which essential oils cause cell death are activation of apoptosis and/or necrosis processes, cell cycle arrest, loss of function of vital organelles, and altering membranes, which may result in reduced ATP production, alteration of the pH gradient, and finally loss of mitochondrial potential, which results in cell death.

The extraction procedure is one of the most important factors influencing essential oil quality. The methods used for extraction are normally dependent on the state and form of botanical material used. The extraction techniques of essential oils can be classified into two sections: traditional and advanced methods. Traditional techniques such as hydro distillation, steam distillation, solvent efficiency, and so forth, however, advanced techniques include subcritical liquid extraction, supercritical fluid extraction and microwave-enhanced methods that increase biological productivity, dissipated time and energy, and increased production yield and high quality of essential oils [6].

2. PROPERTIES OF ESSENTIAL OILS

In a globalized world of sustainable development, essential oils represent a “green” alternative because of their cytotoxic capacity in the pharmaceutical, nutritional, and agricultural fields due to reported antiseptic, expectorant, antifungal, antiviral, insecticidal, antimicrobial, and antioxidant properties, as well as food preservative and stimulation of nervous system [7][8]. Due to the growing demand for organic products, more than 3000 essential oils have been described, out of which only one-tenth is necessary for pharmaceutical, cosmetic and nutritional industries.

The active ingredients in essential oils, which are a complex blend of hydrophobic volatile aroma compounds are given in Figure 1. Which gives them their various physiological implications. Among bioactive compounds of essential oil, monoterpenes represent 80% of the composition, whereas aromatic and oxygenated compounds occur less in essential oil than terpenes. By interfering with the physiological and biochemical processes involved in the development and multiplication of microorganisms, monoterpenoids have an impact on their growth and multiplication. Distinct terpenoid components in essential oils can interact with one another in such a way that they increase or reduce the antimicrobial potency of that respective oil. Effects after interaction between components might be additive, neutral, adversarial, or synergistic. The literature provides extensive information on the biological activities and assessment of essential oils.

2.1. Aromatherapy Properties

Medical herbalism has a vital role in the established area of medicine because it has been the oldest and most broadly used treatment for thousands of years. In today's era of technological and commercial advancement, people experience a wide range of mental and physical issues; as a result, aromatherapy is one complementary therapy used in the pharmaceutical industry that uses

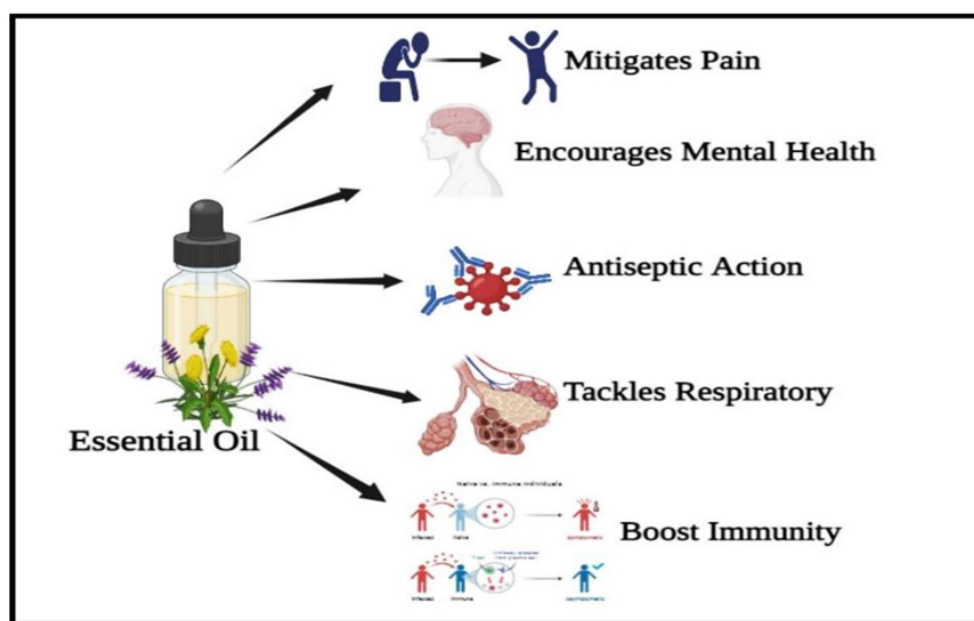


Figure 2. Operating principles of essential oils in aromatherapy [13].

Table 1. Classification, source and mode of action of selected essential oils.

Plant Family	Plant name	Parts of the plant	Chemical compounds of essential oils	Action in aromatherapy	Ref.
Lamiaceae	<i>Hyssopus officinalis</i>	flowers and leaves	β -pinene, pinocamphone, camphor, 1,8-cineole, cubenene	sedative, against allergy	[15]
	<i>Lavandula angustifolia</i>	flowers and leaves	1,8-cineole, borneol, camphor, linalool	reduces the behavioral and emotional signs of dementia in people with Alzheimer's disease, against migraines, reduces stress and anxiety	[16] [17]
	<i>Lavandula latifolia</i>	fresh flowers	α -terpineol, α -bisabolene, eucalyptol, linalool, camphor, α -pinene	relaxation from headache, nose and throat infections	[18]
	<i>Melissa officinalis</i>	dried or fresh leaves and the top aerial section of the plant	citronellal, citronellol, linalool, geraniol	treatment for controlling hemodynamic parameters and stress	[19]
	<i>Salvia sclarea</i>	stems, leaves, flowers, and seeds	linalool, linalyl acetate, geraniol, geranyl acetate, nerol	reduces anxiety, controls high blood pressure, against migraine	[12] [16] [20]
	<i>Rosmarinus Officinalis</i>	leaves	1,8-cineole, camphor, borneol, camphene, limonene, β -caryophyllene, myrcene and α -terpineol	treat bronchitis, headache	[13] [16]
	<i>Pogostemon Cablin</i>	leaves and stems	α - and β -patchoulene, patchoulol, β -caryophyllene, α -guaiene	against migraine, relieving stress	[16]
	<i>Ocimum basilicum</i>	entire plant body	linalool, methyl chavicol, eugenol, bergamotene, methyl cinnamate	treat anxiety, depression, migraine	[13] [16] [21]
	<i>Mentha piperita</i>	flowering parts and leaves	menthol, menthone, thymol, trans-piperitone oxide, spathulenol, 1,8-cineole, limonene, methyl acetate	against migraine, nausea, cold, and flu symptoms	[16] [22] [23]

Table 1. Cont.

Plant Family	Plant name	Parts of the plant	Chemical compounds of essential oils	Action in aromatherapy	Ref.
Myrtaceae	<i>Syzygium aromaticum</i>	stem, leaves, and flowering buds	eugenol, β -caryophyllene, isoeugenol, eugenol acetate, α -humulene	reduces the severity of labor discomfort and anxiety	[24]
	<i>Myrtus communis</i>	leaves and fruits	α -pinene, limonene, 1,8-cineole, linalool, geranyl acetate	reduces the signs of bronchitis, whooping cough, and other respiratory diseases	[16]
	<i>Eucalyptus sp.</i>	leaves	spathuleneol, carvacrol, linalool, α -terpineol, pinocarvone	reduces nasal sneezing, against migraine and inflammation of a mucous membrane	[25] [26]
	<i>Citrus aurantium</i>	fruits, flowers, branches, and leaves	limonene, 4-terpineol, 4-carvomenthenol, linalool, γ -terpinene	analgesics, calming, motor relaxants and antidepressants, treat sour throat activities	[16] [27]- [29]
Rutaceae	<i>Citrus bergamia</i>	fruit peels	limonene, 4-carvomenthenol, linalool, γ -terpinene, β -pinene, linalyl acetate	in opposition to anxiety and stress, provide good sentiments	[30] [31]
	<i>Citrus limon</i>	fruits	limonene, β -pinene, linalyl acetate, α -terpinene, linalool	antistress, antianxiety	[20] [26]
	<i>Citrus sinensis</i>	fruits	limonene, myrcene, α -pinene, linalool, octanal, decanal	against migraine, reduces anxiety	[16] [20]
Santalaceae	<i>Santalum album</i>	wood and roots	α -santalol, β -santalol, bergamotol, nuciferol, lanceol, trans-farnesol	anxiolytic, reduces the effect of drowsiness and hypnosis	[32]
Rosaceae	<i>Rosa damascene</i>	flowers	citronellol, geraniol, nerol, nonadecane, linalool, heneicosane	anti-depressant, to treat cardiac infarction	[13] [32]
Geraniaceae	<i>Pelargonium spp.</i>	shoots and leaves	citronellol, linalool, geraniol, citronellyl formate, p-menthone	anxiolytic	[20]

Table 1. Cont.

Plant Family	Plant name	Parts of the plant	Chemical compounds of essential oils	Action in aromatherapy	Ref.
Asteraceae	<i>Anthemis nobilis</i>	dried flower heads	isobutyl angelate, 2-methyl butyl angelate, 2-methyl butyl isobutyrate, camphene	analgesic, antianxiety	[16]
	<i>Matricaria recutita</i>	whole plants	α -bisabolol oxide, camphene, sabinene, limonene, 1,8-cineole, camphor, α -pinene	reduces whooping cough signs and symptoms respiratory illnesses such as bronchitis	[16]
Oleaceae	<i>Jasminum officinale</i>	flowers and leaves	benzyl acetate, linalool, benzyl alcohol, indole, benzyl benzoate, geraniol	reduces stress	[33]
Apiaceae	<i>Foeniculum vulgare</i>	seeds	trans-anethole, fenchone, estragole, limonene, cis-anethole	treat bronchitis (chest cold)	[13]

essential oils as the primary therapeutic agents to treat a variety of ailments. In 2019, the coronavirus pandemic (COVID-19) became a serious global health concern which caused mental and physical agony which led to the evolution of aromatherapy and therefore, it gained popularity as an alternative treatment for various disorders. However, Jessie Hawkins et al., reported that inhalation of thyme, clove bud, orange, and frankincense essential oils boosts energy levels in post-COVID-19 patients. In this study, forty women were randomized to two groups: placebo and intervention. For fourteen days continuously, the designated product was breathed twice daily by both groups. The Multidimensional Fatigue Symptom Inventory (MFSI) was used to calculate fatigue scores. Fatigue score demonstrates how an exclusive aromatherapy combination can considerably boost energy levels in women who are feeling run down after recovering from COVID-19 [9]-[11]. Once the oils are in the biological system, they remould the immune responses and help the malfunction in the affected location. Olfactory aromatherapy can improve states of mind that are negatively impacted by stress, anxiety, and other life factors. It can also be helpful in physical illnesses

linked to immune system dysfunction, such as cancer, herpes, allergies, asthma, arthritis, skin conditions, and gastrointestinal disorders (such as irritable bowel syndrome). Essential oils can be applied to the skin through a massage or cosmetics. Though cosmetic aromatherapy uses essential oils for the skin, body, face, and hair, it is more difficult to separate the effects of essential oils when they are given topically during massage. The most common aromatherapy delivery method is inhalation. Essential oil inhalation is a quick, effective, and secure technique.

We thrive on performance, competition, and perfection in today's society, which elicits a sneaky rise in stress. Long-term exposure to stress can affect both physical and mental health which can further lead to anxiety, irritability, anger, headaches, and sleeping problems. For combating stress, aromatherapy is one of the holistic approaches, which results in the stimulation of the immune system, reduces tension, and boosts circulation. The use of essential oils during aromatherapy increases breathing rate, and blood oxygen saturation and stabilizes blood pressure, overall it calms the nervous system and helps the

Table 2. Source and bioactive compounds of selected essential oils with antioxidative properties.

Plant Family	Plant Derived Essential oils	Major Chemical Compounds of Essential oils	Assay Methods	Antioxidant Effects	Ref.
Rutaceae	<i>Citrus aurantium</i>	β -pinene, limonene, linalool, α -terpineol, linalyl acetate, geranyl acetate	DPPH, ABTS assay, and collagenase activity	the total phenol content and antioxidant activity of EO are low, 3.48 ± 0.10 mg/g, and $IC_{50} > 10,000$ mg L ⁻¹	[42]
Lamiaceae	<i>Melisa officinalis</i> , <i>Mentha</i> , <i>Ocimum Basilium</i>	geranial, neral, piperitenone oxide, 1,8 cineole, linalool, α -trans bergamotene	DPPH assay	EC_{50} value after 20 min of incubation = 0.68 mg/mL was the highest antioxidant activity shown by basil leaves	[43]
Apiaceae	<i>Cachrys sicula</i>	β -pinene, sabinene, myrcene, α -pinene	ABTS, metal chelating, DPPH assay	in the ABTS technique, the EO antioxidant activity was greater.	[44]
Lamiaceae	<i>Thymus ciliates</i>	myrcene, borneol, geranyl acetate, α -terpinolene, β -ocimene, p-cymene	DPPH and FRAP assay	An IC_{50} of 4.5 g/mL indicated that myrcene has strong antioxidant activity.	[45]
Plantaginaceae	<i>Kickxia aegyptiaca</i>	cuminic aldehyde, caryophyllene oxide, hexahydrofarnesyl acetone, <i>ar</i> -turmerone, aromadendrene oxide	DPPH and ABTS assay	With IC_{50} values for DPPH and ABTS of 30.48 mg L ⁻¹ and 35.01 mg L ⁻¹ , respectively, the K. aegyptiaca EO demonstrated significant antioxidant activity.	[46]
Asteraceae	<i>Artemisia aragonensis</i>	camphor, borneol, 1,8 cineol, and artemisia alcohol	FRAP, DPPH, and TAC assay	significant antioxidant activity as measured by DPPH and FRAP assays, with IC_{50} and EC_{50} values of 0.034 ± 0.004 and 0.118 ± 0.008 mg/mL, respectively.	[47]
Lamiaceae	Six different populations of <i>Origanum heracleoticum</i>	α -pinene, β -myrcene, o-cymene, thymol, γ -muurolene, carvacrol	DPPH and BCBT assays	samples had a low DPPH value of 320.9 μ g/mL and a low BCBT value of 4.68 μ g/mL.	[48]

Table 2. Cont.

Plant Family	Plant Derived Essential oils	Major Chemical Compounds of Essential oils	Assay Methods	Antioxidant Effects	Ref.
Rutaceae	<i>Ruta chalepensis</i>	linalyl acetate, β -linalool, 2-nonanone	DPPH assay	R. chalepensis samples from Jerusalem, Hebron, and Jenin had inhibition percentages of $6.9 \pm 0.94 \mu\text{g/mL}$, 69.56% ; $7.8 \pm 1.05 \mu\text{g/mL}$, 61.53% ; and $19.9 \pm 0.68 \mu\text{g/mL}$, 24.12% , respectively.	[49]
Cyperaceae	<i>Cyperus rotundus</i>	cyperene, α -selinene, α -cyperone, (d)-limonene	DPPH, BCBT, and ABTS radicals scavenging activity	ABTS radicals were substantially higher than Trolox ($84.7 \mu\text{g/mL}$), whereas DPPH radicals were significantly lower ($13.1 \mu\text{g/mL}$) than Trolox.	[50]
Apiaceae, Lamiaceae	<i>Foeniculum vulgare</i> , <i>Petroselinum crispum</i> , <i>Lavandula officinalis</i>	limonene, anethole, fenchone, linalool, linalyl acetate, <i>trans</i> - β -ocymene, myristicin, apiole, α -pinene, β -pinene	DPPH and FRAP assays	given the highest percentage of suppression of the DPPH radical (64.28%) and FRAP (0.93 mmol/L Trolox), P. crispum had the best antioxidant profile.	[51]
Euphorbiaceae	<i>Jatropha gossypifolia</i>	phytol, γ -cadinene, α -aromadendrene, β -bisabolene, germacrene D, limonene	DPPH, nitric oxide, ABTS, lipid peroxyl	the antiradical strength of the stem was higher in comparison to the leaf EO.	[52]
Apiaceae, Piperaceae, Liliaceae, Brassicaceae, Zingiberaceae	<i>Coriandrum sativum</i> , <i>Piper nigrum</i> , <i>Cuminum cyminum</i> , <i>Allium sativum</i> , <i>Brassica nigra</i> , <i>Allium cepa</i> , <i>Curcuma</i>	cumin and coriander seed oil, linalool, <i>p</i> -coumaric acid	DPPH	the antioxidant profile of mustard is $155.16 \mu\text{g/mL}$, cumin is $163.50 \mu\text{g/mL}$, and coriander is $150.62 \mu\text{g/mL}$.	[53]

body feel relaxed (Table 1). Due to the existence of essential or volatile oils, it has been observed that several plants can be used in aromatherapy such as *Jasminum officinal*, *Ocimum basilicum*, *Lavandula*

officinalis, *Rosa damascene*, *Cananga odorata* and *Anthemis nobilis* are most common plants used to cure anxiety [12]. The application of essential oils can be in the form of a vapor balm, nasal inhaler,

lamp diffusion techniques, room sprays (air fresheners), or direct inhalation (a tissue or cotton ball with a few drops of essential oil). Aromatherapy is excellent at relieving stress and tension, improving mood, promoting balance and well-being, soothing minor aches and pains, and enhancing the immunological, respiratory, and circulatory systems as shown in Figure 2 [13].

As a result, aromatherapy is a secure, organic gift from nature to humans. Aside from removing sickness symptoms, aromatherapy also revitalizes the complete body. Additionally, essential oils can be divided into seven classes based on their aroma [14].

2.2. Food Preservative Properties

Food is undoubtedly necessary for survival. In fact, according to the World Health Organisation (WHO), consuming tainted food causes 1 in 10 people to become unwell every day [34]. Through the creation of novel, non-toxic preservatives with significant antioxidant and antimicrobial characteristics, new societal and economic insinuations drive an urgent need for safer food [35] [36]. There is a growing tendency toward the use of natural and safer preservatives, giving food an image of being natural or green/organic. Particular attention has focused on the applications of plant essential oils as food preservatives because of their

non-carcinogenic and hypoallergenic nature along with oxidative deterioration reduction potential. Essential oils show strong antibacterial and food preservation qualities, which offer the food, sector significant potential. The primary barriers to employing essential oils as food preservatives include their safety restrictions, noticeable organoleptic effects, and potential contamination by chemical products like pesticides. Accordingly, many essential oils and the United States Food and Drug Administration (FDA) and the European Commission approved the use of these natural ingredients, classifying them as generally recognized as safe (GRAS) for use in food products as flavorings and/or preservatives [37][38]. Loss of organoleptic quality and nutritious content of the food is a desired outcome of microbial and enzyme inactivation. As a result, it is crucial to create efficient storage techniques and alternative technologies to protect and enhance food storage quality and shelf life. The unstable nature (less solubility with high instability) and pungent aroma of essential oils make them problematic for use as a direct food preservative which can alter the aroma and other organoleptic aspects of fresh produce when used simply.

William Oyom's and his co-researchers indicate that modified sweet potato starch incorporated with cumin essential oil can be considered a suitable

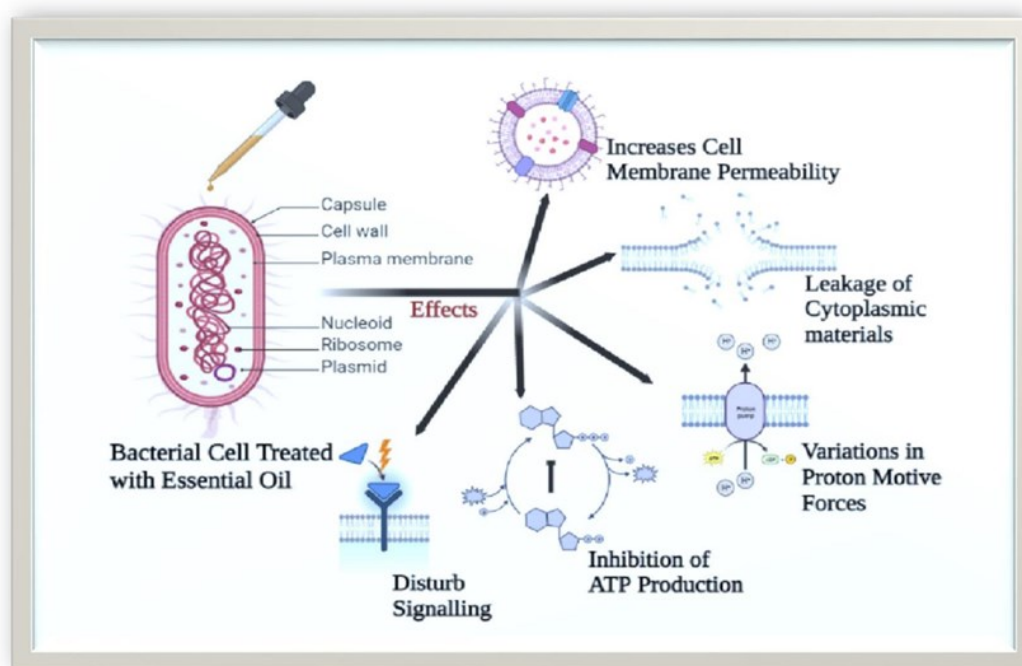


Figure 3. Action mode of essential oils on the bacterial cell.

Table 3. Anticyanobacterial activity of essential oils against harmful Cyanobacteria.

Model organism	Essential oil extracted from	Result	Conclusion	Ref.
<i>Microcystis aeruginosa</i> , <i>Cyanobium gracile</i> , <i>Trichormus variabilis</i> , <i>Dolichospermum circinale</i> .	<i>Deinococcus metallilatus</i> and <i>Deinococcus radiodurans</i> .	the lethal rate of <i>M. aeruginosa</i> increases with an increase in the concentration of deinoxanthin compounds.	the production of deinoxanthin compounds using agricultural by-products could be a sustainable cyanobacterial bloom-removing strategy.	[62]
<i>Microcystis aeruginosa</i>	rice straw aqueous extract.	the chlorophyll-a as one of the primary photosynthetic pigments in cells was damaged due to rice straw aqueous extract.	it provides an alternative sustainable technology for controlling the growth of harmful algal blooms.	[63]
<i>Cochlodinium polykrikoides</i>	<i>Satureja khuzistanica</i> , <i>Satureja rechingeri</i> , <i>Zataria multiflora</i> .	the stability of the essential oil of <i>S. khuzistanica</i> was higher in the experimental environment.	the features which make a compound favorable as an inhibitor include high effectiveness, low toxicity, and low cost.	[64]
<i>Microcystis aeruginosa</i>	<i>Artemisia annua</i> , <i>Conyza Canadensis</i> , <i>Erigeron annuus</i>	the ethyl acetate, petroleum ether, and ethanol extracts from these composite plants have the potential to be utilized for control and mitigation of algal bloom.	the world-wide distribution of Compositae plants can also allow obtaining algicidal constituent.	[65]
<i>Microcystis aeruginosa</i>	40 medicinal plants (China)	a significant decrease in total microcystin concentration was found in all treatment groups compared to control.	selected medicinal plants have no damaging effect on human health, have no toxic side effects, are economical, and causing no pollution.	[66]

composite coating for preserving and maintaining the quality of climacteric fruits stored at ambient conditions [39]. When it comes to fruit juice, Raybaudi Massilia, Mosqueda-Melgar, and Martin-Belloso (2006) found that lemongrass essential oil (EO) and geraniol were effective at preventing the

growth of *Listeria* sp., *Escherichia coli*, and *Salmonella* sp. in pear, melon, and apple juices [40]. As essential oils have potent antibacterial properties against food-borne microorganisms, which the food industry can utilize as a preservative or an antimicrobial ingredient in food packaging.

2.3. Antioxidant Properties

Reactive oxygen species (ROS) are a group of damaging molecules that include singlet oxygen, superoxide ions, hydroxyl ions, and hydrogen peroxide. When there is an imbalance between free radicals and antioxidant defences, then free radical oxidizing agent damages DNA, membranes, and enzymes, which can result in several diseases in humans, including cancer, atherosclerosis, malaria, coronavirus disease (COVID-19), rheumatoid arthritis, and neurological conditions. Antioxidant properties of essential oils due to their chemical components are considered to inhibit lipid peroxidation and to save from damage due to free radicals (Table 2). Antioxidants can suppress oxidation chain reactions, which can be the origin of free radicals, which can also lead to cancer, atherosclerosis, and aging [41].

2.4. Antimicrobial Efficacy

Pathogenic microorganisms have developed a resistance to antibiotics so that they can be environmentally safe, there has been increased interest in biologically active chemicals that have been extracted from plant species in recent years to eradicate pathogenic germs [54]. Numerous chemical substances with antimicrobial characteristics are produced by plants; some of these substances are consistently present, whereas others are secreted in reaction to stressors including infection, injury, predators, and changes in the

weather. Certain studies have shown that many of the phenols, aldehydes, ketones, alcohols, esters, or hydrocarbons included in essential oils exhibit exceptional antimicrobial properties when tested separately, and that activity derives from the intricate interactions between the many classes of chemicals. The antimicrobial activity of essential oils can be certified by in-vitro study; diverse methods are used to investigate the antimicrobial activities of essential oils. The agar or broth dilution, agar diffusion, and vapor phase test are the most crucial ones. In this way, using essential oils to manage pathogenic microbes that are multi-drug resistant can be sufficiently used to conflict with various infectious diseases [55]. The antimicrobial efficacy of essential oil is based on the type of microbe to be suppressed as well as the evaluation techniques, such as dilution, difference, and bio-autography [56].

2.4.1. Antibacterial Properties

Studies regarding essential oils antibacterial properties against the pathogens, illustrate a growing interest in bio-control methods instead of conventional synthetic antibiotics. Disease caused due to bacteria on plants may lead to significant economic impact. The majority of research on the antibacterial capabilities of essential oils has been done in the context of food preservation or health concerns. Most essential oils show a higher antibacterial effect against Gram-positive bacteria

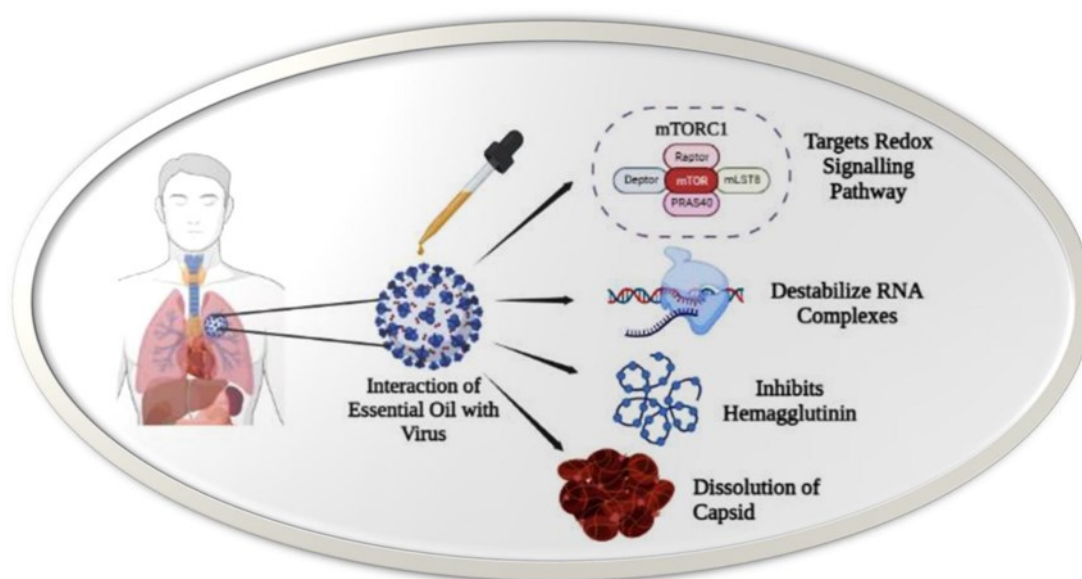


Figure 4. Phases of viral-cycle influenced by essential oil.

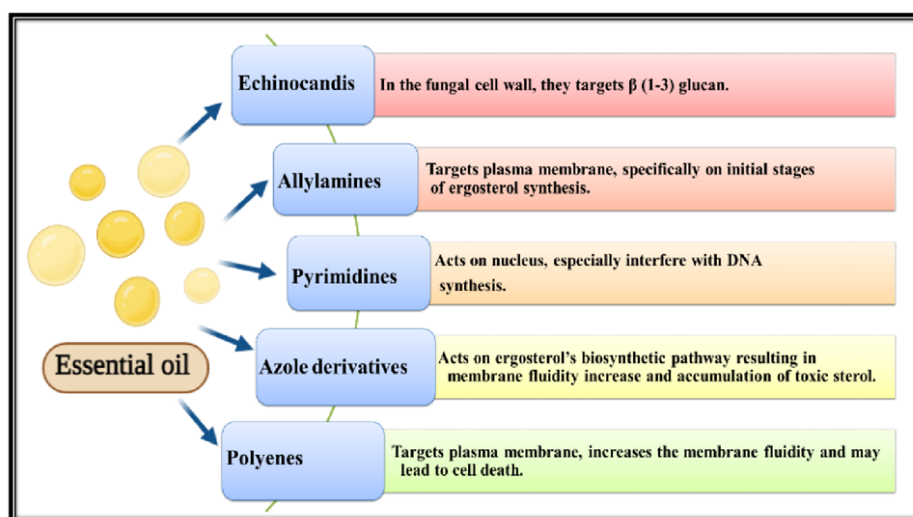


Figure. 5 Major Compounds of Essential Oils and their Antifungal Action [75].

in comparison to Gram-negative bacteria. For example, *Chrysopogon zizanioides* and *Santalum album* essential oils show higher inhibitory effects against the Gram-positive bacterial strains but no inhibitory effects against Gram-negative bacterial strains (*Pseudomonas aeruginosa* ATCC 9027, *Escherichia coli* O157:H7 ATCC 4389). Essential oils and their compounds are endowed with the important quality of hydrophobicity. This enables essential oils to separate through the lipids found in bacterial cell membranes and mitochondria, ultimately resulting in the death of bacterial cells due to the effusion of important ions and molecules from bacterial cells. An antibacterial property was associated with the frequency of the main bioactive like eugenol, carvacrol, and p-cymene. The antibacterial effect of essential oils was related to diminished membrane potentials, proton pumps, and ATP destruction. Similarly, tea tree oil suppresses the progress of *S. aureus* and *E. coli* by changing cellular permeation, enhancing the depletion of inner cellular potassium ions, and disrupting the organization of un-similar fatty acids, lipids, and polysaccharides substances [57]. Figure 3 shows the essential oil mechanism of action of an antibacterial including inhibitions of metabolic pathways, protein synthesis, nucleic acid synthesis, and cell wall formation.

Multidrug-resistant bacterial strains such as *Acinetobacter baumannii* and *Pseudomonas aeruginosa* whose action was inhibited by geraniol which was identified as an active compound of the essential oils and significantly increased the

efficacy of various antibiotic classes, including β -lactams and quinolones and act as efflux pump inhibitors [58]. *Helicobacter pylori* colonies infectious were treated with EO of *Thymus caramanicus* and *Apium nodiflorum* to control the infection, and as a result of the experiment, their respective MIC values were 12.5 g/mL and 14.5 – 58.0 g/mL [59][60].

2.4.2. Anticyanobacterial Properties

Excessive growth of toxin-producing blue-green algae in a water body leads to the formation of harmful cyanobacterial bloom. The growth and spread of cyanobacteria are influenced by a variety of abiotic and biotic variables. The driving impetus behind the formation and spread of cyanobacterial blooms, according to researchers, are anthropogenic eutrophication and climate change. Control of cyanobacterial blooms is crucial and urgently needed because the proliferation of cyanobacteria limits transparency and light penetration into the aquatic ecosystem, which has an impact on the growth of primary benthic producers. Cyanobacterial blooms could be eliminated or controlled by using several physical, chemical, and biological techniques which affect their morphological and physiological characteristics.

As prospective synthetic algicidal agents, natural compounds derived from a variety of organisms, such as seaweeds, plants, and microorganisms, have been studied. Since the isolates used in the research were cultivated in a completely different environment from the wild strains, the results may

change in the actual environment. Many factors are considered when it comes to field trials, like, the area of the experimental site, location, and climatic conditions, to maintain laboratory conditions such as temperature, pH, and photoperiod, are highly challengeable. The mitigation process is hampered by other biological components that are present in the environment. There is an urgent need for additional study on the efficiency of control agents, particularly for harmful cyanobacterial blooms and their interactions with other species and aquatic life. A wide variety of cyanobacterial species are still unexplored. Cyanotoxins are produced by bloom-forming cyanobacteria such *Microcystis*, *Anabaena*, and *Planktothrix*. The generation of cyanotoxins by stressed cyanobacteria may enhance the risk to the environment and human health as a result of changing aquatic environmental conditions. Controlling cyanobacteria before they bloom can lessen the dangers cyanotoxins present to human health. Only widespread applications of essential oils that have undergone thorough testing and are ecologically sound should be regarded as feasible (Table 3) [61].

2.4.3. Antiviral Properties

According to existing biochemical and molecular biological tests, the described in vitro and in vivo research highlight the baseline data about the most recent discoveries of the antiviral and virucidal effects of essential oils on enveloped and non-enveloped viruses. Rapid screening and isolation of bioactive individuals, which is necessary for the discovery and development of novel antiviral drugs, can be accomplished. Essential oils are lipophilic by nature so, their antiviral effects most likely alter or obstruct viral membrane proteins that are necessary for host-cell attachment [66]. According to the literature survey, numerous essential oils have been proven to have antiviral properties against a variety of RNA and DNA viruses, including the type 1 and type 2 herpes simplex viruses (HSV-1 and HSV-2), type 2 dengue viruses, type 3 adenovirus, Junin virus, poliovirus and coxsackie virus B1. The essential oil from *Salvia desoleana Atzei* and *Vincenzo Picci* substantially reduced the acyclovir-resistant HSV-2 strains with an effective concentration value (IC_{50}) of 28.57g/mL, a significantly lower concentration than that of

acyclovir (71.84 g/mL). Further, reported an inhibition of herpes virus replication and prevention of cell-to-cell spread by using *Santolina insularis* EO in vitro. Certain types of non-enveloped DNA and RNA viruses, such as the poliovirus, coxsackie virus B1, and adenovirus type 3, are resistant to the antiviral effects of *Syzygium aromaticum* and *Origanum vulgare* essential oils [67]. It's interesting that some ingredients, including 1,8-cinole and eugenol, are ineffective against HSV-1 yet have high anti-influenza properties. Other oxygen-bearing substances including terpinen-4-ol and α -santalol have also been reported to be important bioactive substances against influenza virus (IFV). This discordant finding suggests that some components of anti-HSV and anti-influenza properties may be additive. A hypothesis that has to be verified is that non-oxygenated terpene hydrocarbons are more efficient against HSV and oxygenated terpenes against IFV. WHO officially announced the pandemic on March 11th, 2020 [68]-[73] and at that time no antiviral treatment and vaccines were available against the corona virus. In such a circumstance, a broad spectrum such as essential oil seems relevant.

Envelope viruses are protected by a lipid membrane allowing them to be safe from the eyes of the immune system. To attack a wrapped virus, a fat-soluble active ingredient is needed. Essential oils are fat-soluble therefore; the virus is affected by the intracellular action of essential oils at various stages during its life cycle such as inhibition of replication by changing the spatial conformation of their proteins or by replacing hydroxyl group of these proteins as given in Figure 4. A cell can resist viral infiltration and adsorption by attaching aromatic molecules to virus receptors. Through in silico analysis, antiviral and virucidal molecules in essential oils have been discovered that can prevent the entry of viruses into our cells. Another benefit of using this analysis is for estimating the binding affinity of essential oil compounds to viral/ host cell proteins to explain and demonstrate their biological effects. Using the molecular docking method, it was possible to demonstrate that many compounds (e.g., isothermal, organosulfur compounds, 1,8-cineole, jensenone, and others) may exert relatively strong binding to the viral and host cell-specific target molecules that are crucial for virus-cell adsorption

Table 4. Action mechanism of essential oils against pathogenic fungi in plants and humans.

Targeted fungi	Disease caused by fungi	Essential oil extracted from	Mechanism of action	Ref.
<i>Alternaria solani</i>	early blight	<i>Angelica archangelica</i>	antifungal	[79]
<i>Aspergillus flavus</i>	rot and mold, aflatoxins production, aspergillosis	<i>Mentha x piperita</i> , <i>Origanum spp.</i> , <i>Rosmarinus officinalis</i> L., <i>Schinus mole</i> L. and <i>Tagetes minuta</i> L.	effect on membrane	[80]
<i>Claviceps purpurea</i>	ergotism	<i>Ocimum basilicum</i> and <i>Vetiveria zizanioides</i>	inhibition of mycelia growth	[81]
<i>Colletotrichum capsici</i>	leaf spot	<i>Juniperus Sabina</i>	suppression of spore germination	[82]
		<i>Cestrum nocturnum</i>	effect on spore germination	[83]
		<i>Metasequoia glyptostroboides</i>	antifungal	[84]
		<i>Piper chaba</i>	effect on spore germination	[85]
		18 Egyptian plant species	inhibition of mycelia growth and spore germination	[86]
<i>Fusarium oxysporum</i>	Fusarium wilt (vascular disease)	<i>Metasequoia glyptostroboides</i>	antifungal	[87]
		<i>Eucalyptus erythrocytes</i>	growth inhibition	[88]
<i>Fusarium verticillioides</i>	oesophageal tumors	<i>Zingiber officinale</i> , <i>Cinnamomum zeylanicum</i> , <i>Cymbopogon martini</i>	structural damage to the fungal cell wall, decreased conidia size, and mycelial reduction.	[89]
<i>Penicillium spp.</i> , <i>Aspergillus spp.</i>	cardiac beriberi	<i>Cymbopogon martini</i> <i>Melaleuca alternifolia</i> <i>Illicium verum</i>	effect on membrane	[90]
<i>Penicillium italicum</i>	blue mold	<i>Thymus spp.</i>	inhibition of spore germination	[91]
		<i>Rosmarinus officinalis</i>	inhibits spore germination	[92]
<i>Phytophthora infestans</i>	late blight	<i>Citrus sinensis</i> <i>Cadenera</i> , <i>Citrus limon</i> <i>Eureka</i> , and <i>Citrus bergamia</i> <i>Castagnaro</i>	inhibitory effects on sporulation, mycelial growth	[93]
		<i>Thymus spp.</i>	antifungal	[94]
		<i>Origanum majorana</i> L.	synergistic/ antagonistic	[95]
<i>Pythium spp.</i>	root rot	<i>Thymus spp.</i>	inhibiting mycelium development	[96]
		<i>Mikania scandens</i>	antifungal	[97]
<i>Vaginal candidiasis</i>	vaginal infection	<i>Syzygium aromaticum</i>	antifungal	[98]
		<i>Pelargonium graveolens</i>	antifungal	[99]

(ACE2, TMPRSS2, RBD), penetration/internalization (RBD), and replication (Mpro) [74].

2.4.4. Antifungal Properties

Fungi have vast economic importance like in antibiotics production and agriculture by maintaining soil fertility. However, fungi are also responsible for threats to both agricultural production and the health of immune-compromised as well as healthy individuals. Fungi cause huge economic losses to agriculture; they are responsible for nearly 30% of all crop diseases. In Figure 5, echinocandis allylamines, pyrimidines, azole derivatives, and polyenes are major constituents of essential oils with antifungal properties.

Numerous scientific studies have emphasized the significance and consequently, the contribution of numerous plant families, such as Asteraceae, Liliaceae, Apocynaceae, Solanaceae, Rutaceae, Piperaceae, etc., used as healthy plants [76]. Fungi directly damage the host plants and animals by producing mycotoxins such as aflatoxins (carcinogens). Control of phytopathogenic fungi such as *Alternaria*, *Botrytis*, *Fusarium*, *Penicillium*, and *Rhizoctonia* are the most studied ones. Due to the presence of phytochemical components, the EO shows antifungal activity [75]. Several methods used to evaluate the antifungal effects of essential oils were the serial broth or agar dilution, poisoned food test, disk diffusion, spore germination, examination of nuclear condensation, and detection of damage to the plasma membrane. As essential oils contain useful compounds, few are described in the table that increase their value in the research area (Table 4) [77]. The most prevalent fungus-related illnesses that affect people include aspergillosis, candidiasis, and mold infections caused by *Scedosporium* spp, *mucorales*, *Fusarium* spp, *Aspergillus* spp, and *Candida* can be controlled by treating with Essential oils of *Cinnamomum zeylanicum*, *Cymbopogon citrates*, *Mentha piperita*, *Melaleuca alternifolia*, etc. [78].

3. CONCLUSIONS

Essential oils are frequently described as the plant's inherent essence. They are natural hydrophobic plant products containing a complex mixture of components, especially terpenoids. The

advancement of essential oils is based on their potential as versatile bioactive molecules. The research on the antimicrobial activity of essential oils makes it quite obvious that these substances are endowed with special antibacterial, antifungal, and antiviral capabilities and therefore, can be used as antimicrobial agents. Under the volatile and low toxicity nature essential oils persistency is lower than that of synthetic chemicals, so, essential oils are easy, less expensive, environmentally beneficial and biodegradable to use on a global level. The application of essential oils promotes sustained healing and reduces stress without any adverse side effects. Despite being used in the medical, nutritional, and agricultural fields due to their antimicrobial properties, essential oils cannot substitute the usage of synthetic goods meanwhile when compared to commercial treatments, essential oils' antibacterial effects against some microbial strains are not as potent. Recovering from COVID-19 by the application of essential oils provides a novel, non-invasive approach to improving quality of life and is beneficial for mental endurance. Moreover, the advancement of systems of biochemistry coupled with biotechnology for employing green substitutes might help rural farmers and consumers in developing countries to meet the demand for eco-friendly goods. Essential oils remain a strong prospect for future treatments, but there is still a tremendous of work that must be done before we can truly incorporate them into the current pharmaceutical, nutritional, and agricultural sectors.

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N.S., R.S., R.P. and N.A. made substantial contributions to the conception of the work and drafted the work; N.S. made a contribution in preparing figures and the tables of the manuscript; Sh.Y. and K.N.T. reviewed the manuscript with the inputs from other co-authors; T.K. and Sa.Y. edited the manuscript and approved the version to be published with input from other co-authors.

Conflicts of Interest

The authors declare no conflict of interest.

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